Multiple Treatment Cycles of Neural Stem Cell Delivered Oncolytic Adenovirus for the Treatment of Glioblastoma.

Journal: Cancers (Basel)

Publication Year: 2021

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PubMed link: 34944938

Public Summary:
The human body's ten trillion cells are constantly assailed with environmental insults and genetic susceptibilities that can initiate tumor formation. Yet, most people live cancer-free for decades. This bewildering feat is due, in part, to the remarkable ability of our immune system to recognize and eliminate tumor cells. Unfortunately, 12,000 Americans/year are diagnosed with a rare, aggressive, and fatal tumor that escapes immune recognition: glioblastoma. Here, we continue efforts to develop a treatment capable of stimulating immune recognition of glioblastoma. The treatment is based on an oncolytic virus that causes tumor-selective infections. Neural stem cells are used to enhance viral distribution throughout the tumor. This study selects a dosing strategy to enable more comprehensive viral inoculation of the tumor than was possible in our previous clinical trial. This research demonstrates to the broader community that multiple-cycle oncolytic virotherapy may be therapeutically beneficial despite an anti-viral response after the first administration.

Scientific Abstract:
Tumor tropic neural stem cells (NSCs) can improve the anti-tumor efficacy of oncovirotherapy agents by protecting them from rapid clearance by the immune system and delivering them to multiple distant tumor sites. We recently completed a first-in-human trial assessing the safety of a single intracerebral dose of NSC-delivered CRAd-Survivin-pk7 (NSC.CRAd-S-pk7) combined with radiation and chemotherapy in newly diagnosed high-grade glioma patients. The maximum feasible dose was determined to be 150 million NSC.CRAd-Sp-k7 (1.875 x 10(11) viral particles). Higher doses were not assessed due to volume limitations for intracerebral administration and the inability to further concentrate the study agent. It is possible that therapeutic efficacy could be maximized by administering even higher doses. Here, we report IND-enabling studies in which an improvement in treatment efficacy is achieved in immunocompetent mice by administering multiple treatment cycles intracerebrally. The results imply that pre-existing immunity does not preclude therapeutic benefits attainable by administering multiple rounds of an oncolytic adenovirus directly into the brain.